II. REMARKS:

A. Status of the Claims

Claims 1-14 were originally filed with the application. All claims were rejected in an Office Action mailed February 22, 2002. In a Response mailed on May 9, 2002, claims 1-7 were cancelled and claim 9 was amended. The remaining claims, claims 8-14, were rejected in a Final Office Action mailed August 27, 2002. Claim 8 was amended in a Response mailed on October 24, 2002. An Advisory Action was mailed on December 4, 2002, in which it was stated that the amendment to claim 8 was not entered because it raised new issues that would require further consideration and/or search. It was also stated in the Advisory Action that the proposed amendment would be entered upon the filing of an appeal. A Request for Continued Examination (RCE) was filed on January 20, 2003. Thus, claims 8-14 were pending at the time of the present Action.

All pending claims are rejected in the outstanding Office Action, mailed on February 13, 2003. Claims 11-14 are cancelled herein, claim 8 is amended herein and claims 15-26 are added herein. It was unclear to Applicant whether the amendment to claim 8 made in response to the Final Office Action was entered upon filing of the RCE application. Therefore, that amendment, along with additional amendments to claim 8, is being re-submitted herein. Support for the amendments to claim 8 can be found throughout the specification, particularly at page 5, lines 13-15. Support for added claims 15-21 can be

found throughout the specification, particularly at page 12, lines 8-24. Support for added claims 22-26 can be found throughout the specification, particularly at page 11, lines 11-16.

B. The Claims are Not Anticipated by Takeda Chemical

Claims 8, 9, 11 and 12 are rejected under § 102(b) as being anticipated by Takeda Chemical. Takeda is said to teach the use of the claimed neurotrophic factor stimulator in a pharmaceutical formulation for the treatment of neuropathy and retinal diseases. Applicant respectfully traverses.

Applicant first points out that the rejection is moot with respect to claims 11 and 12 due to their cancellation herein. The present invention is directed to a method of treating retina or optic nerve head neuropathy associated with glaucoma by administering a composition containing one or more non-peptide neurotrophic factor stimulators, where the composition is administered topically or intraocularly (See claim 8). Takeda, on the other hand, describes a compound (idebenone) that inhibits generation of superoxide and is used to treat diabetic complications. There is no mention within Takeda of the use of a neurotrophic factor stimulator to treat retina or optic nerve head neuropathy associated with glaucoma. Furthermore, the compound in Takeda is administered only systemically. There is no mention within Takeda of topical ophthalmic or intraocular administration of a neurotrophic factor stimulator to treat retina or optic nerve head neuropathy associated with glaucoma.

It is well known that, for a prior art reference to render a claim anticipated, that reference must set forth every element in the claim, either expressly or inherently. *Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 631, 2 U.S.P.Q.2d 1051 (Fed. Cir. 1987) (citing *Connell*

v. Sears, Roebuck & Co., 722 F.2d 1542, 1548, 220 U.S.P.Q. 193, 198 (Fed. Cir. 1983)). In other words, to support a rejection under section 102, a reference must show ***all*** features of the rejected claim(s). *Minnesota Mining & Mfg. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1569, 24 USPQ2d 1321 (Fed. Cir. 1992). The Federal Circuit has stated that "absence of a claim element from a prior art reference negates anticipation." *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 224 U.S.P.Q. 409 (Fed. Cir. 1984). Since Takeda clearly lacks a teaching of several elements of the claimed invention, namely, the topical or intraocular administration of neurotrophic factor stimulators to treat retina or optic nerve head neuropathy associated with glaucoma, it is submitted that Takeda cannot be said to anticipate the claimed invention.

In light of the foregoing, Applicant respectfully requests that the anticipation rejection based on Takeda be withdrawn.

C. The Claims are Not Anticipated by Yan *et al.*

Claims 8, 11 and 12 are rejected under § 102(b) as being anticipated by Yan, *et al.* Yan is said to teach the use of a neurotrophic factor for the treatment of retina or optic neuropathy caused by glaucoma. Applicant respectfully traverses.

Applicant first points out that the rejection is moot with respect to claims 11 and 12 due to their cancellation herein. Applicant would agree with the Examiner's assessment that Yan teaches the use of a (specific) neurotrophic factor for the treatment of injury or degeneration of retinal ganglion cells. In fact, Yan appears to teach the administration of a protein product derived from glial cell line-derived neurotrophic factor (GDNF) to treat such

disorders. The present invention, on the other hand, is directed to a method of treating retina or optic nerve head neuropathy associated with glaucoma, and other retinal conditions, by administering a composition containing one or more non-peptide neurotrophic factor stimulators (See claim 8).

Careful study of the disclosure in Yan revealed no teaching of the use of a non-peptide neurotrophic factor stimulator to treat retina or optic nerve head neuropathy, AMD, retinal ischemia, acute retinopathies associated with trauma, post-surgical complications, damage associated with ocular laser therapy including photodynamic therapy (PDT), or surgical light induced iatrogenic retinopathy, as is required by the present invention. Rather, Yan appears only to teach the administration of compositions containing a protein product derived from a specific neurotrophic factor, which is quite different from a non-peptide neurotrophic factor stimulator. It is well known among those of skill in the art that peptide molecules are difficult to exploit pharmaceutically due to bioavailability problems generally resident in the pharmaceutical administration of peptides. (Spec. page 5, lines 10-13). Thus, focusing on the use of non-peptide molecules which stimulate neurotrophic activity in compromised retinal tissues, without the bioavailability problems attendant to the natural peptides is an object of the present invention. (Spec. page 5, lines 13-15).

Applicant reiterates that to support a rejection under section 102, a reference must show ***all*** features of the rejected claim(s) (*Minnesota Mining & Mfg.* 976 F.2d at 1569) and that "absence of a claim element from a prior art reference negates anticipation," (*Atlas Powder* 224 U.S.P.Q. at 411). Since Yan clearly lacks a teaching of several elements of the claimed

invention, namely the use of non-peptide neurotrophic factor stimulators to treat retinal or optic nerve head neuropathy associated with glaucoma, AMD, retinal ischemia, acute retinopathies associated with trauma, post-surgical complications, damage associated with ocular laser therapy including photodynamic therapy (PDT), or surgical light induced iatrogenic retinopathy, it is submitted that Yan cannot anticipate the claimed invention.

In light of the foregoing arguments, Applicant respectfully requests that the anticipation rejection based on Yan be withdrawn.

D. The Claims are Not Obvious Over Rathbone *et al.* in view of Yan

The Action next rejects claims 10 and 14 under § 103 as being obvious over Rathbone *et al.* in view of Yan. Rathbone is said to teach the use of the claimed neurotrophic factor, AIT-082, in a pharmaceutical formulation as a neuroprotective agent. The Action acknowledges that Rathbone lacks a teaching of the use of the compound for protection of retina or optic nerve and different routes of administration. Yan is said to teach that neurotrophic factors have been previously used for the treatment of retina or optic neuropathy caused by glaucoma and that they can be used by oral or topical administration. Thus, the Action asserts that the skilled artisan would have been motivated to combine the teachings of Rathbone and Yan, "since one relates to the use of the claimed compound as a neurotrophic stimulator and the other relates to the use of neurotrophic stimulators in the treatment of retina or optic head neuropathy." Applicant respectfully traverses.

Applicant first points out that, in fact, the two references relied upon to support the obviousness rejection discuss different subject matter. That is, one discusses protein products

from a neurotrophic factor (GDNF), while the other discusses a particular neurotrophic factor stimulator (AIT-082). As the Action recognizes, although the primary reference discusses the use of a neurotrophic factor stimulator, AIT-082, it lacks a teaching of the use of that neurotrophic factor stimulator in any ophthalmic diseases, much less in the treatment of retina or optic nerve head neuropathy associate with glaucoma, AMD, retinal ischemia, acute retinopathies associated with trauma, post-surgical complications, damage associated with ocular laser therapy including photodynamic therapy (PDT), or surgical light induced iatrogenic retinopathy. Rather, Rathbone discusses the use of AIT-082 only in treatment of nervous system disorders, such as Alzheimer's disease or acute neuronal injuries due to trauma and stroke. There is no suggestion within Rathbone that AIT-082 might be useful in the treatment of retina disorders.

As stated above, Yan does not contain a teaching of a neurotrophic factor stimulator, but rather of a neurotrophic factor, which is a protein. Yan discloses the use of protein products derived from GDNF to treat injury or degeneration of retinal ganglion cells. There is no suggestion within Yan to use non-peptide neurotrophic factor stimulators, as is required by the present invention, to treat retinal disorders.

Determining obviousness requires an analysis of the invention *as a whole*. *Gillette Co. v. S.C. Johnson & Son, Inc.*, 919 F.2d 720, 724 (Fed. Cir. 1990). Significantly, *Gillette* emphasizes that whether all of the elements of the claimed invention were old in other contexts is immaterial to the issue of obviousness. Rather, "*what must be found obvious to defeat the patent is the claimed combination.*" *Id.* (quoting *Kimberly-Clark Corp. v. Johnson*

& Johnson, 745 F.2d 1437, 1448, 223 U.S.P.Q. 603, 609-10 (Fed. Cir. 1984)) (emphasis in original). In the present case, what must be found is the use of non-peptide neurotrophic factor stimulators to treat retina or optic nerve head neuropathy associate with glaucoma, AMD, retinal ischemia, acute retinopathies associated with trauma, post-surgical complications, damage associated with ocular laser therapy including photodynamic therapy (PDT), or surgical light induced iatrogenic retinopathy.

It is well settled patent law that "obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art." *See In re Fine*, 837 F.2d 1071, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988); *In re Jones*, 958 F.2d 347, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992); MPEP § 2143.01. In this case, it is not a matter of merely substituting "one neurotrophic stimulator for another," as the Action suggests. Only one of the cited references contains a teaching of a neurotrophic factor stimulator, and that reference does not suggest the use of that neurotrophic factor stimulator to treat any ophthalmic disorders. The other cited reference teaches only the use of protein products derived from a specific neurotrophic factor. There is no mention within the secondary reference of the use of neurotrophic factor stimulators, much less of the use of non-peptide molecules. Therefore, there clearly exists no motivation to combine the teachings of the cited references. Even if one did combine their teaching, one would not arrive at the claimed invention.

In light of the foregoing, Applicant respectfully requests that the obviousness rejection based on Rathbone in view of Yan be withdrawn.

E. Conclusion

This is submitted to be a complete response to the outstanding Action. Based on the foregoing arguments, the claims are believed to be in condition for allowance; a notice of allowability is therefore respectfully requested.

The Examiner is invited to contact the undersigned attorney at (817) 551-4321 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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